



LEBANESE SOCIETY OF
GASTROENTEROLOGY

الجمعية اللبنانية
لأمراض الجهاز الهضمي

Inflammatory Bowel Diseases: LEBANESE GUIDELINES

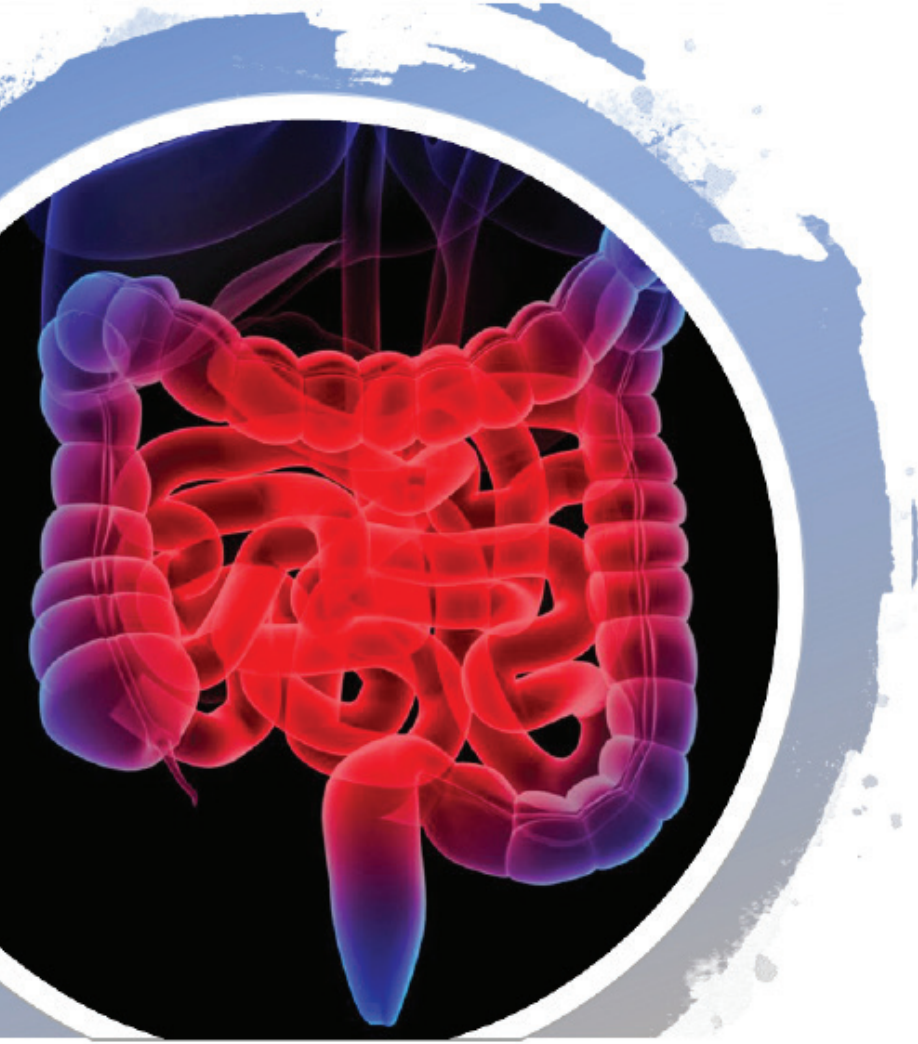


TABLE OF CONTENTS

I- Crohn's Disease:	Page 4-9
1. Definitions	Page 4
2. Management of Active Uncomplicated Luminal (Inflammatory) CD	Page 5-6
3. Peri-anal (fistulizing) Crohn's Disease	Page 7-8
4. Post-operative Crohn's Disease	Page 9
II- Ulcerative colitis:	Page 10-15
1. Definitions	Page 10
2. Disease Distribution and Disease Activity	Page 10-11
3. Management	Page 11-15
III- Extra-Intestinal Manifestations in Inflammatory Bowel Diseases	Page 16
IV- Inflammatory Bowel Disease in Pregnancy	Page 17-19
V- General and Practical Instructions for Vaccinations	Page 20-21

CROHN'S DISEASE

1. Definitions

Clinical Remission:

Resolution of symptoms (normal stool frequency, no abdominal pain, no perianal pain or drainage)

Endoscopic Remission:

Absent or minimal endoscopic lesions

No Response:

No clinical improvement within 2-3 weeks of corticosteroid therapy, or up to 12 weeks of anti-TNF therapy

Relapse:

Flare of symptoms associated with evidence of inflammation as determined by CRP, fecal calprotectin, MR or CT enterography, endoscopy or ultrasound and absence of viral/bacterial infection

Recurrence:

The reappearance of lesions after surgical resection

Steroid-resistant:

Patients who have active disease despite prednisone of up to 0.75 mg/kg/day over a period of 4 weeks

Steroid-dependent:

Patients who are either

- Unable to reduce steroids below the equivalent of prednisolone 10 mg/day within 3 months of starting steroids without recurrent active disease, or
- Who have a relapse within 3 months of stopping steroids

2. Management of Active Uncomplicated Luminal (Inflammatory) CD

Algorithms 1 and 2

Disease activity is assessed clinically by the CDAI or the Harvey-Bradshaw Index.

Endoscopic disease activity is assessed by the SES-CD

Mildly Active Localized ileocecal CD

- Oral Budesonide is the preferred treatment. No maintenance treatment is an option for some patients with isolated mild disease, minimal symptoms and endoscopic findings
- Because of limited evidence of efficacy compared to placebo, oral mesalamine should not be used to treat patients with active Crohn's disease. Similarly, metronidazole and/or ciprofloxacin have no role in patients with uncomplicated luminal CD
- For patients who relapse or have recurrent or persistent symptoms, an immunomodulator should be considered to maintain steroid-induced remission

Moderately Active Localized Luminal CD

- Moderately active localized luminal Crohn's disease should be treated with systemic corticosteroids. Azathioprine, methotrexate, or biologics (Infliximab, Adalimumab, Vedolizumab, or Ustekinumab) should be considered for maintenance after steroid-induced remission in patients who relapse or are steroid-dependent
- Biologics should be used for induction and maintenance of remission in steroid-refractory or intolerant individuals
- Biologics (Infliximab, Adalimumab, Vedolizumab or Ustekinumab) should be considered as first-line in patients with extensive anatomic involvement including the foregut (stomach/duodenum/jejunum) or with other unfavorable risk factors such as young age (<30 years) of disease onset, presence of deep ulcers, perianal disease, prior surgical resection, and structuring or penetrating disease (refer to the fistulizing CD guideline recommendations)

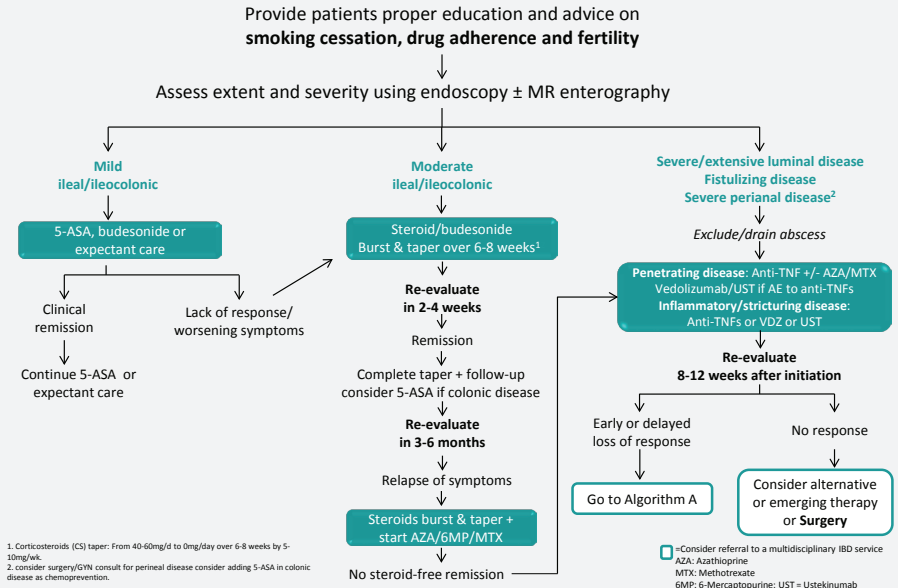
Severely Active Localized Luminal CD

- Severely active localized luminal Crohn's disease should initially be treated with systemic corticosteroids and/or biologics (Infliximab, Adalimumab, Vedolizumab or Ustekinumab) taking into consideration disease severity, location (foregut involvement) and risk factors
- In the case of Infliximab and possibly Adalimumab, combination with an immunomodulator is recommended particularly in the first 6-12 months of treatment. Reduced dose Azathioprine (1-2 mg/kg) and Methotrexate (12.5-15 mg wee-kly) may be sufficient when used in combination with anti-TNFs. There is no evidence to date to support the addition of immunomodulators to Vedolizumab or Ustekinumab
- Surgery is also an option for localized short segment CD and should be discussed with patients. Refer to the postoperative CD guidelines for management of disease recurrence

Regardless of treatment regimen, a treat-to-target strategy is recommended with serial clinical, biochemical (CRP and fecal calprotectin), and endoscopic and/or radiologic assessment of disease activity

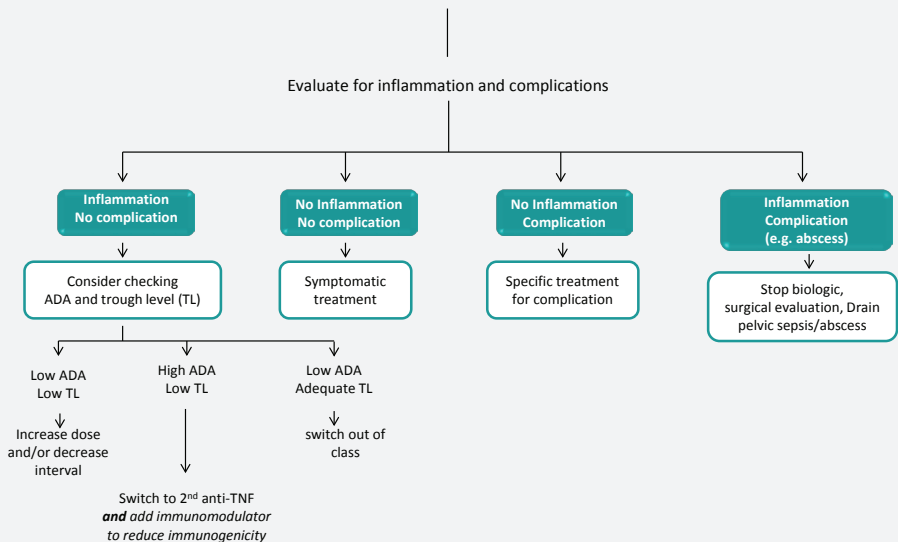
Algorithm 1: Treatment for Crohn's Disease

Treatment Algorithm for Crohn's Disease



Algorithm 2: Loss of Response to 1st Anti-TNF Agent

Loss of Response to 1st Anti-TNF Agent



ADA: Anti-Drug Antibodies
TL: Trough Level

3. Peri-anal (fistulizing) Crohn's disease

Figure 1, Algorithm 3

Fistula Classification

- Simple fistulas are low, below the dentate line, and include superficial, intersphincteric, or intrasphincteric fistulas, with a single external opening without other complications
- Complex fistulas are high, arising above the dentate line, and may have multiple external openings or involvement of adjacent organs (recto vaginal fistula, recto vesical fistula)
They may be associated with perianal abscesses, rectal stricture, proctitis, or connections with the bladder or vagina

Diagnosis and Assessment

- Contrast-enhanced pelvic magnetic resonance imaging (MRI) is considered the initial procedure for the assessment of perianal fistulizing CD
- If rectal stenosis is excluded, endoscopic anorectal ultrasound (EUS) is a good alternative
- Specificity and sensitivity of both imaging modalities is increased when combined with examination under anesthesia
- Fistulography is not recommended

Management

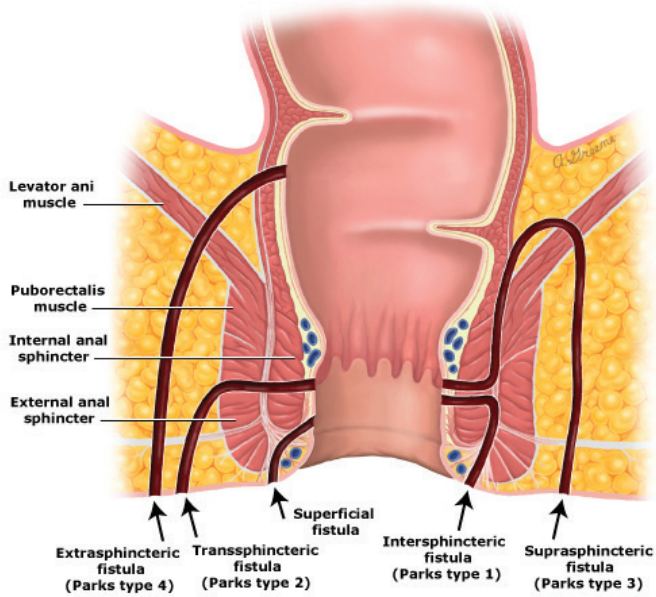
DRUGS USED IN PERIANAL FISTULIZING CROHN'S DISEASE

- Antibiotics (ciprofloxacin and metronidazole) are used to treat perianal sepsis and act as an effective bridge to immunosuppressive therapy
- There is no role for steroids in perianal Crohn's disease
- Thiopurines can be used for the treatment of perianal fistulas in patients with CD following antibiotics and drainage
- Biologic Agents
 - Infliximab is considered the gold-standard therapy for patients with perianal fistulas
 - Adalimumab is an alternative therapy
 - Vedolizumab or Ustekinumab are second line options after failure or intolerance to anti TNF

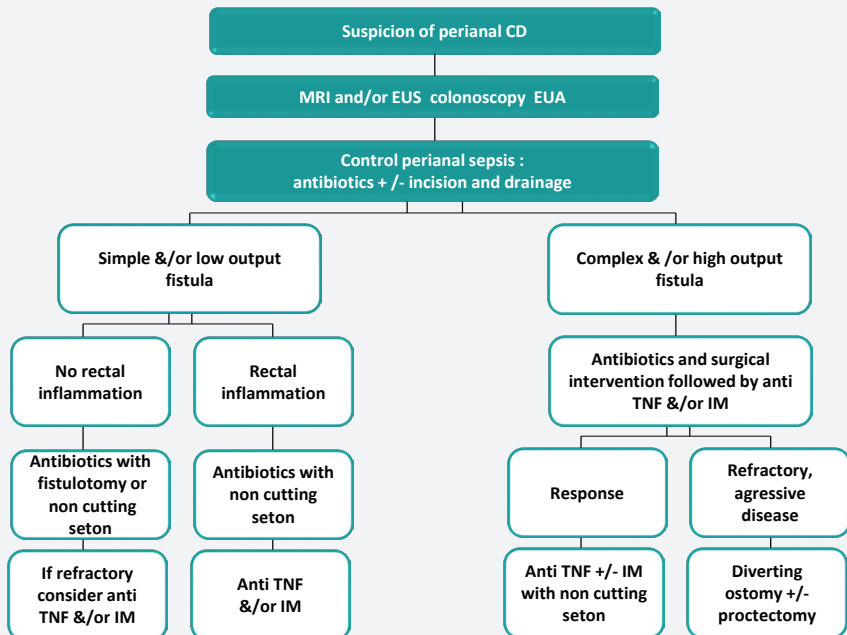
MANAGEMENT OF FISTULAS

- Superficial fistula can be treated with fistulotomy
- Any other type of fistulae with abscess should be treated by surgical drainage and non-cutting seton placement
- Simple perianal fistulas should benefit from antibiotic use as first line therapy (Ciprofloxacin and Metronidazole)
- In refractory or recurrent fistulas not responding to antibiotics, Thiopurines and /or Anti TNF alpha should be used as second line therapy
- In complex perianal fistulizing disease, Infliximab or Adalimumab could be used as first line therapy along with antibiotics with or without Thiopurines
- Active luminal Crohn's disease should be treated if present along with fistula treatment
- Thiopurines, Infliximab or Adalimumab in combination with seton drainage or alone should be used as maintenance therapy
- Timing of seton removal depends on the effects of the medical therapy. If no pus or stool drainage is obtained, seton could be removed
- Patients refractory to medical therapy should be considered for a diverting ostomy and proctectomy as the last resort

Figure 1: Parks Classification System of Perianal Fistulas.



Algorithm 3: Peri- Anal (Fistulizing) Crohn's Disease



4. Post-operative Crohn's Disease

Table 1, Algorithm 4

RECOMMENDATIONS

- Ileocolonoscopy 6-12 months postoperatively should be performed to assess for endoscopic recurrence
- Presence of symptoms and or elevation of Calprotectin (>150) and/or CRP within the first 6 months post-operatively should prompt earlier intervention and treatment

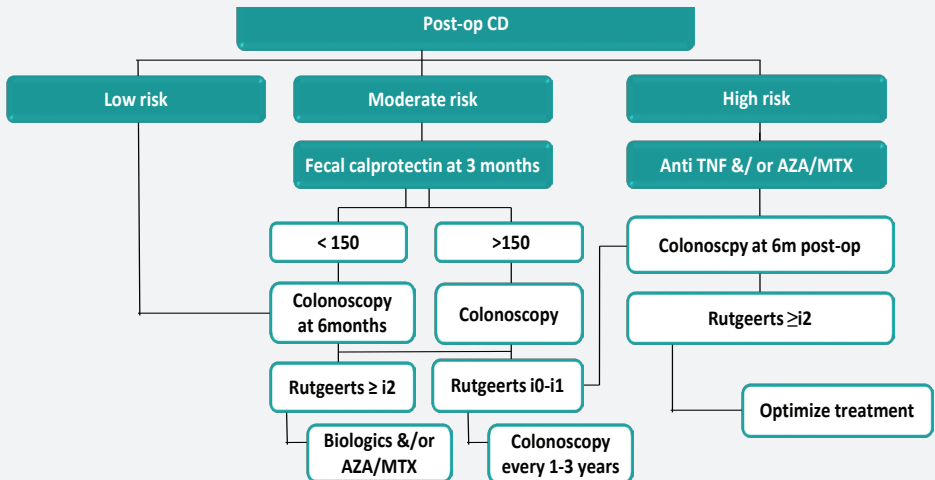
MANAGEMENT OF POSTOPERATIVE CD

- High risk patients are those with penetrating disease, smokers, or patients who have had at least 2 intestinal resection surgeries
- Moderate-risk patients are those with a longer segment of diseased bowel (>10 cm) and/or who have had a short time to surgery (<10 years)
- Low risk patients are non-smokers with no penetrating/fistulizing disease who are undergoing their first intestinal resection surgery
- Rutgeerts endoscopic score is used to direct therapy

Table 1. Rutgeerts Endoscopic Recurrence Scoring System

Endoscopic Score	Definition
i0	No lesions
i1	≤5 aphthous lesions
i2	>5 aphthous lesions with normal mucosa between the lesions or skip areas of larger lesions confined to the ileocolonic anastomosis
i3	Diffuse aphthous ileitis with diffusely inflamed mucosa
i4	Diffuse inflammation with already larger ulcers, nodules and/or narrowing

Algorithm 4: Post-Operative Crohn's Disease



ULCERATIVE COLITIS

1. Definitions

Clinical Remission:

Resolution of symptoms (stool frequency ≤ 3 /day, no bleeding and no urgency)

Endoscopic Remission:

Absent or minimal endoscopic lesions

Relapse:

Flare of symptoms (blood in stool, tenesmus, diarrhea) with or without evidence of mucosal inflammation and in the absence of concomitant infection

Steroid-resistant:

Patients who have active disease despite prednisone of up to 0.75mg/kg/day over a period of 4 weeks

Steroid-dependent:

Patients who are either

- Unable to reduce steroids below the equivalent of prednisolone 10 mg/day within 3 months of starting steroids, without recurrent active disease, or
- Who have a relapse within 3 months of stopping steroids

2. Disease Distribution and Disease Activity

Algorithm 5

Proctitis:

Involvement is limited to the rectum (i.e. the proximal extent of inflammation is distal to the recto-sigmoid junction)

Left Sided Colitis:

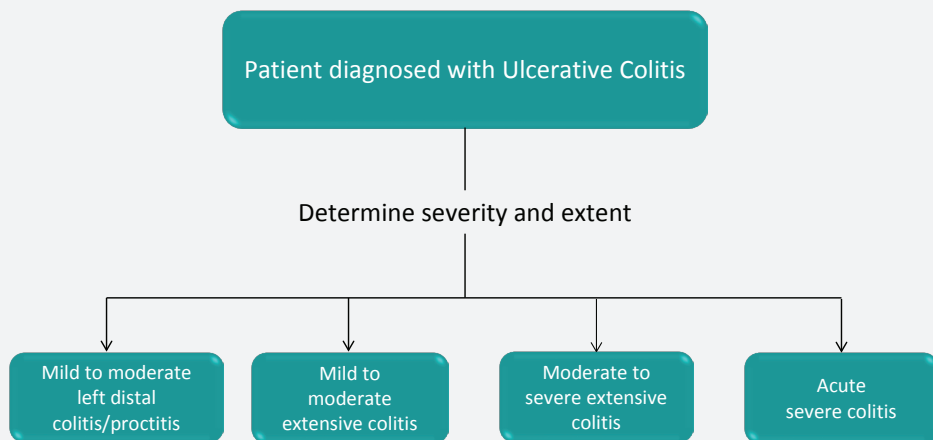
Involvement is limited to the portion of the colon distal to the splenic flexure

Extended Colitis:

Involvement extends beyond the splenic flexure and includes pan-colitis

Clinical disease severity can be assessed by the Partial Mayo Score or a Full Mayo Score (includes endoscopy). The severity of an acute exacerbation of UC can be assessed using the criteria of Truelove and Witts

Evaluation Pathway for Ulcerative Colitis



3. Management

INDUCTION OF REMISSION

Mild to Moderate Proctitis/Proctosigmoiditis: *Algorithm 6*

- Topical treatment with mesalamine is the first-line therapy
- The preferred treatment is 1-g per day Mesalamine suppositories
- Topical steroids can be used as a second-line therapy or as an alternative for patients with intolerance to topical Mesalamine
- Using topical 5-ASA or topical corticosteroids in combination with oral 5-ASA (≥ 2 g/day is more effective than using it individually and should be considered for the escalation of treatment
- Evaluation of treatment response is recommended after 4-8 weeks of oral/rectal 5-ASA induction therapy to determine the need to modify therapy
- Patients who fail to respond require additional treatment with oral prednisone burst and taper (greater or equal 40m/day)

Mild to Moderate Left-Sided Colitis: *Algorithm 7*

- Combination of topical mesalamine enemas and oral mesalamine > 2 g/day should be the first option
- Use of systemic steroids needs to be addressed at the latest 2 to 4 weeks if treatment failure

3. Management

Mild to Moderate Extensive Colitis: *Algorithm 7*

- Combined therapy using oral and topical 5-ASA medication is superior to the single use of either of them
- Budesonide MMX could be considered for patients with suboptimal response to 5-ASA treatment
- Systemic corticosteroids should be considered earlier for those with extensive colitis and/or treatment failure, especially for patients considered for maintenance immunomodulatory therapy
- Treatment with Biologics (Infliximab, Adalimumab, Golimumab, Vedolizumab, Tofacitinib or Ustekinumab) is recommended in Corticosteroid-Resistant Mild to Moderate UC or when adequate dosage and duration of treatment with corticosteroid does not improve symptoms (after 2 to 4 weeks), or if the treatment is not tolerated by the patient

Moderate to Severe UC: *Algorithm 8*

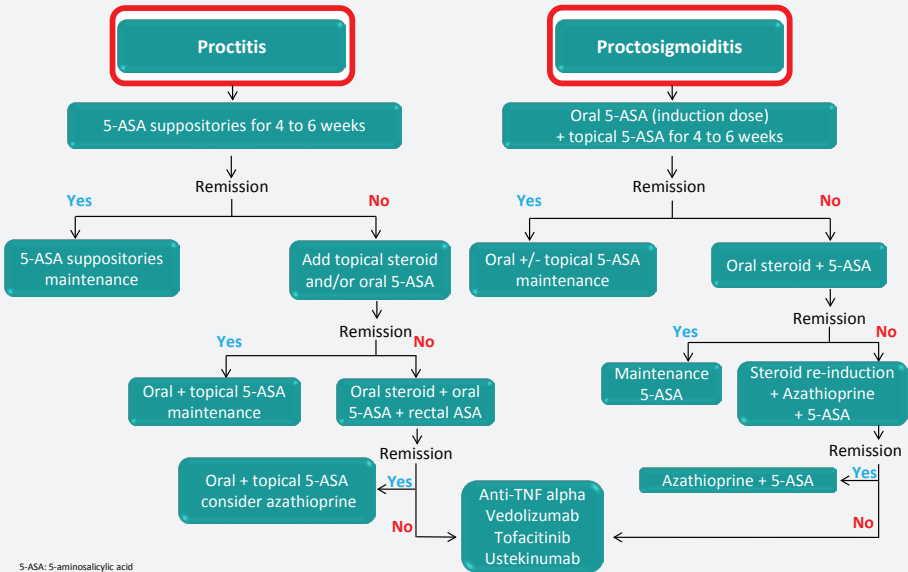
- Oral corticosteroid administration is recommended as the initial treatment to induce remission in Moderate to severe UC
- Biologics (Infliximab, Adalimumab, Golimumab, Vedolizumab, Tofacitinib, Ustekinumab) are recommended when adequate dosage and duration of treatment with corticosteroid does not improve symptoms (after 2 to 4 weeks), or if the treatment is not tolerated by the patient

Severe Ulcerative Colitis of Any Extent: *Algorithm 9*

- Patients generally require hospitalization
- Infection should be excluded (CMV, C. Difficile, Amebiasis, etc.)
- Surgical consultation should be obtained
- Steroid therapy is still the gold standard with an initial intravenous dose of 1 mg/kg.
- Prophylaxis against venous thromboembolism should be given
- Treatment strategy must be revised if no improvement is seen or symptoms are worsening after 72h
- In case of failure of steroids, options include the calcineurin inhibitors (cyclosporine or tacrolimus) or the anti-TNF Infliximab
- Colectomy is considered if a patient with intravenous corticosteroid-refractory severe UC presents aggravation of clinical symptoms or does not respond to biologics or IV cyclosporine treatment

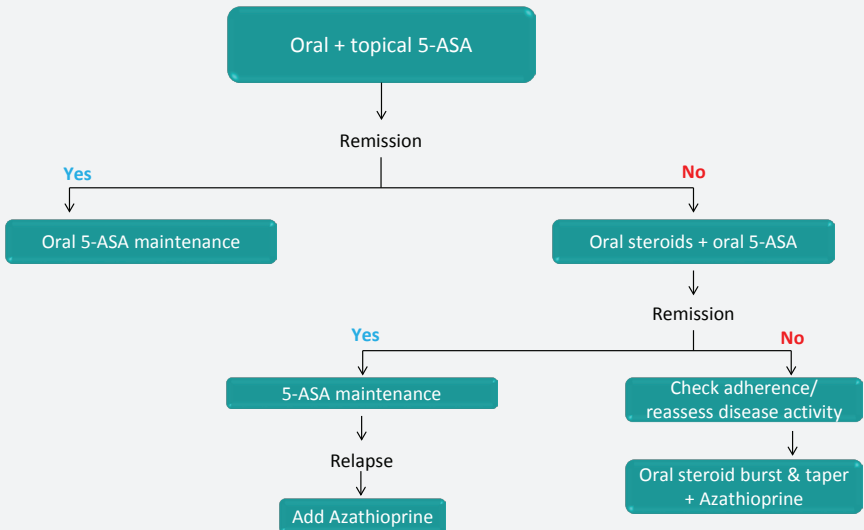
Algorithm 6: Management of Mild to Moderate Distal

Mild to Moderate Distal Colitis



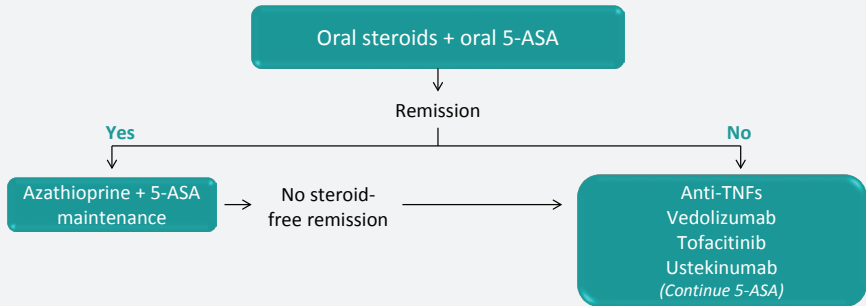
Algorithm 7: Management of Mild to Moderate Extensive Colitis

Mild to Moderate Extensive Colitis



Algorithm 8: Management of Moderate to Severe Extensive Colitis

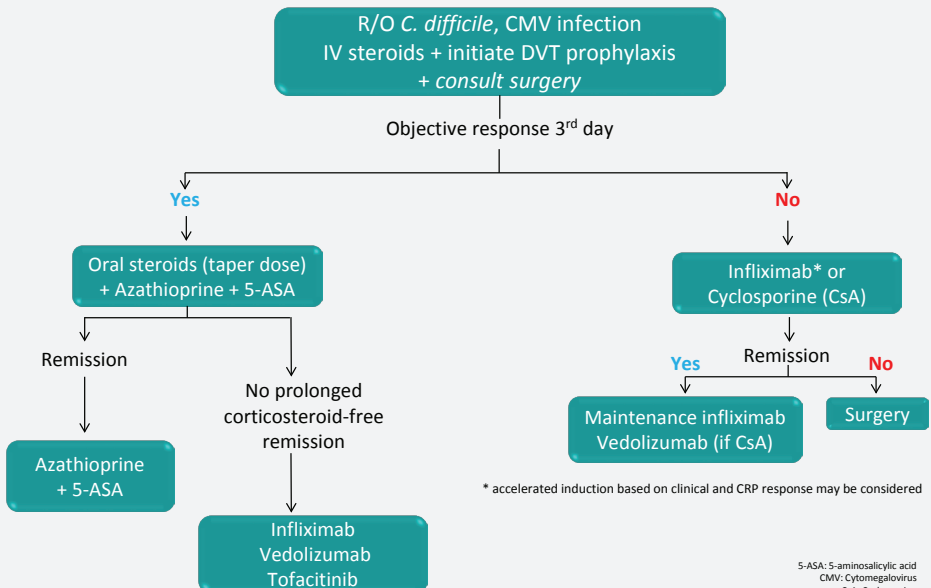
Moderate to Severe Extensive Colitis



5-ASA: 5-aminosalicylic acid

Algorithm 9: Management of Acute Severe Ulcerative Colitis

Acute Severe Ulcerative Colitis



5-ASA: 5-aminosalicylic acid
CMV: Cytomegalovirus
CsA: Cyclosporine
DVT: Deep Venous Thrombosis

MAINTENANCE OF REMISSION

Proctitis

- A topical aminosalicylate alone is generally sufficient (daily or intermittent dosing)

Proctosigmoiditis, Left-sided and Extensive Ulcerative Colitis

- Maintenance should be with oral aminosalicylate ($\geq 2\text{g/day}$) in combination with topical 5-ASA treatment (daily or intermittent dosing)
- Thiopurine or Biologics (Infliximab, Adalimumab, Golimumab, Vedolizumab, Tofacitinib, Ustekinumab) are recommended in patients with early or frequent relapses despite taking adequate dosage of 5-ASA, and in those who are unable to take 5-ASA
- In patients who showed clinical remission with corticosteroids, Thiopurine or Biologics can be used to maintain remission
- Thiopurine or Biologics are recommended in patients with corticosteroid-dependent UC

Absolute Indications of Surgery for UC

- Uncontrolled bleeding
 - Perforation
 - Malignancy
 - Severe UC that does not respond to medical treatment
 - Toxic megacolon
 - Uncontrolled symptoms
 - Cases where continuous medication is impossible because of adverse effects
- The standard surgery for UC is total proctocolectomy and ileal pouch-anal anastomosis (IPAA)
 - A 3-step procedure is recommended in all patients receiving biologics within 12 weeks of surgery

EXTRA-INTESTINAL MANIFESTATIONS IN INFLAMMATORY BOWEL DISEASES

Management

Bone and Joint Disease:

- Arthropathy and Arthritis should be jointly managed with rheumatologists
- Patients receiving prolonged tapered (more than 3 months) systemic steroid therapy should receive calcium and vitamin D for the duration of treatment
- NSAIDs should not be used in IBD patients. Short courses of celecoxib in UC patient

Eye Disease:

- Simple episcleritis, uveitis and scleritis, should be treated by an ophthalmologist with expertise in ocular inflammatory disease

Skin Disease:

- Erythema nodosum:
 - Treatment is usually based on that of the underlying IBD
 - Systemic corticosteroids are required in severe cases
 - Relapsing and resistant forms can be treated with immunomodulators or anti-TNF
- Pyoderma gangrenosum
 - treated with systemic corticosteroids, Infliximab or Adalimumab, or topical or oral calcineurin inhibitors

Hepatobiliary Disease:

- Primary Sclerosing Cholangitis
 - Ursodeoxycholic acid [15–20mg/kg/d] improves serum liver tests without evidence of benefits on outcomes
 - Corticosteroids and/or immunosuppressers should be considered in patients with features of AIH
 - ERC is recommended to diagnose strictures that may be amenable to endoscopic dilatation] and for brush cytology specimen evaluation

Venous Thromboembolism:

Prophylaxis is recommended for all IBD patients admitted to the hospital. It should be considered also following discharge from the hospital, after recent surgeries, and in outpatients with severe active disease

INFLAMMATORY BOWEL DISEASE IN PREGNANCY

Table 2

Inflammatory Bowel Disease Concerns:

- Having active disease is associated with a significant increase in the rate of preterm birth
- When perianal active disease is present, there is up to a 10-fold increased risk for fourth-degree laceration

Medications:

- Aminosalicylates (except sulfasalazine), biologics, or thiopurine can be continued during pregnancy and through delivery
- Corticosteroids can be utilized as an adjunctive therapy for disease flares but should be avoided for maintenance therapy
- Combination therapy utilizing biologics and thiopurine is discouraged. Monotherapy with biologics is preferred
- Starting thiopurine therapy for the first time in pregnancy is not recommended
- Continuation of biologic therapy in pregnancy is recommended (available data for anti TNF, case by case discussion for other biologics)
- In order to minimize trans-placental transfer near the time of delivery, the administration of biologics can be delayed during the 3rd trimester, especially in patients with long term remission
- Pregnant women hospitalized for IBD are candidates for anticoagulation prophylaxis

Delivery Plan:

- Vaginal delivery is recommended in IBD patients, unless active perineal disease is present
- Cesarean section is the recommended mode of delivery for women with prior recto-vaginal fistulas

Post-delivery Care for Mother:

- Biologics may be resumed 24 hours after vaginal delivery and 48 hours after cesarean delivery
- Other IBD-specific medications should be continued in the post-partum period
- The majority of the medications prescribed for IBD are either undetectable in breast milk or are present in such low concentrations that they would not be expected to cause harm to the breastfeeding infant

Vaccination Recommendations for the Newborn:

- If the mother is exposed to any biologic therapy (other than certolizumab) during the third trimester of pregnancy, avoidance of live vaccines is recommended for the first six months of life
- The varicella (VZV) and measles, mumps, rubella (MMR) live vaccines, which are given at one year of age, are acceptable to administer

Table 2: Inflammatory Bowel Disease Drug and Pregnancy

AMINOSALICYLATES	Maintain pre-pregnancy dosing	
Mesalamine	All preparations are now phthalate free	Compatible with breastfeeding <ul style="list-style-type: none"> ▪ No preparation preference ▪ Monitor infant for diarrhea
IMMUNOMODULATORS	Dosing may be altered due to increased renal clearance with pregnancy. Therapeutic drug monitoring recommended	Routine infant therapeutic drug monitoring not necessary
Cyclosporine (calcineurin inhibitor)	Limited data in pregnancy suggest associations with hypertension, gestational diabetes, preterm birth, low birth weight	Safe in breastfeeding
Thiopurines (azathioprine, 6-mercaptopurine)	<ul style="list-style-type: none"> ▪ Continue as monotherapy ▪ Consider cessation of thiopurine as combination therapy given possible association with increased infant infections ▪ Use with caution in combination with allopurinol, which carries potential embryo toxic effects 	Compatible with breastfeeding
Methotrexate	Contraindicated. Stop 3 months prior to conception	Not advised
SMALL MOLECULES		
Tofacitinib	Limited human data. Consider other options, particularly in first trimester	Not advised
BIOLOGICS	<ul style="list-style-type: none"> ▪ Maintain pre-pregnancy dosing ▪ Continue dosing throughout all three trimesters ▪ If possible, plan final dose according to drug half-life to minimize transfer <ul style="list-style-type: none"> - Drug dosed every 4 weeks give 4-6 weeks prior to delivery - Drug dosed every 8 weeks give 8-10 weeks prior to delivery - If accelerated dosing, time dose for trough 	Compatible with breastfeeding

Table 2: Inflammatory Bowel Disease Drug and Pregnancy

Adalimumab	Plan final pregnancy injection 3-2 weeks prior to EDC and resume post-partum	
Certolizumab pegol	May continue scheduled dosing throughout pregnancy	
Golimumab	Plan final pregnancy infusion 6-4 weeks prior to EDC and resume post-partum	
Infliximab	Plan final pregnancy infusion 10-6 weeks prior to EDC and resume post-partum. Base dosing on pre-pregnancy weight during pregnancy and immediate post-partum	
Ustekinumab	Plan final pregnancy infusion 10-6 weeks prior to EDC and resume post-partum	
Vedolizumab	Plan final pregnancy infusion 10-6 weeks prior to EDC and resume post-partum	
CORTICOSTEROIDS	Reserved for active flares in pregnancy Not recommended for maintenance therapy during pregnancy	Compatible with breastfeeding <ul style="list-style-type: none"> ▪ Subtherapeutic infant exposure expected, even with flare dosing
ANTIBIOTICS	Reserved for perianal disease and pouchitis and not recommended for planned maintenance therapy (amoxicillin/metronidazole preferred over ciprofloxacin)	<ul style="list-style-type: none"> ▪ Amoxicillin/clavulanic acid compatible with breastfeeding ▪ Ciprofloxacin preferred over metronidazole

GENERAL AND PRACTICAL INSTRUCTIONS FOR VACCINATIONS

Recommendations Apply to all Patients Considered for Treatment with

- Systemic corticosteroids, more than 20 mg of prednisone equivalent per day for more than 2 weeks
- All immunomodulators and biologics

In Case of Immunosuppression

- Live vaccines are contraindicated
- Inactivated or recombinant vaccines are allowed

The Main Live Attenuated Vaccines Contraindicated in Case of Immunosuppression

BCG - MMR - Rotavirus - Varicella and HZV - Yellow fever - Oral polio - Influenza (only nasal allowed)

The Inactivated or Recombinant Vaccines Authorized

Diphtheria, tetanus, subcutaneous polio, whooping cough, typhoid fever, meningococcus A and C, pneumococcus, hemophilus, leptospirosis, influenza injectable, HPV, HBV, HAV

If Vaccination with a Live Vaccine is Considered, Refer to *Algorithm 10*

Vaccination Recommendations

1. Practice the reminders provided by the immunization schedule
2. Vaccinate HBV for non-immune and at-risk patients
3. Vaccine against VZV non-immune patients
4. Vaccinate against yellow fever patients who visit an endemic area
5. Vaccinate against HPV girls and women (<19 years) and men who have sex with men (<26 years)

Vaccination Recommendations in Immunocompromised Patients

1. Seasonal flu: every year
2. Pneumococcus according to the following scheme:
 - A. Absence of previous vaccination: one dose of 13-valent conjugate vaccine (Pevnar)(PCV13) followed at least 8 weeks later by one dose of 23-valent polysaccharide vaccine (pneumo 23) (PPV23)
 - B. Previous vaccination only with PPV23> 1 year: a dose of PCV13 then PPV23 at least 5 years after the previous dose of PPV23
 - C. Vaccination with the PCV13 - VPP23 sequence: reminder by VPP23 after 5 years

SCREENING FOR LATENT INFECTIONS

Tuberculosis Screening

- Screening and treatment of active or latent TB infection (LTBI) are fundamental and should be done in all patients
- Chest radiography is important to exclude active TB and to provide additional evidence of LTBI
- Tuberculin skin test (PPD) is recommended as first test. However, IGRA (quantiferon) is the preferred first-line test in patients receiving steroids or immunomodulators or who have a history of BCG vaccination

Hepatitis B and C Screening *Table 3*

Human Immunodeficiency Virus (HIV) *Table 3*

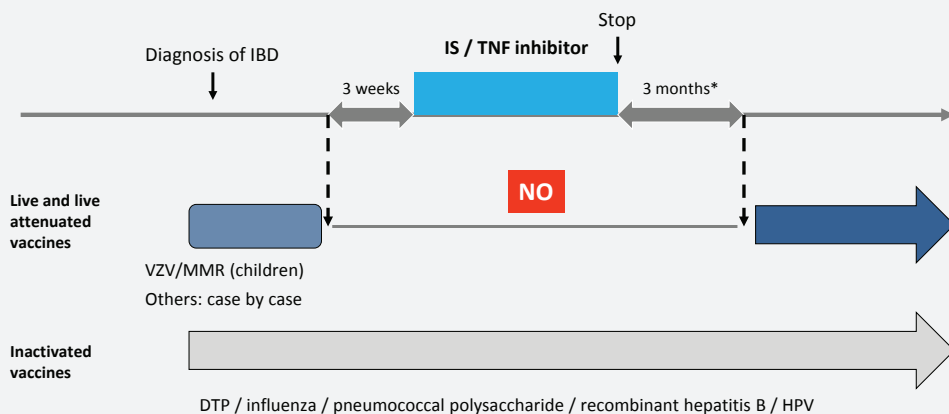
Table 3: Pre Biologic Check List

Pre-biologic Check List

Laboratory work-up	Special considerations
Hepatitis B virus - HBs antigen, anti-HBs and -anti-HBc	
Hepatitis C virus (anti-Hepatitis C) antibody	
Human immunodeficiency virus (anti-HIV)	
Epstein–Barr virus (anti-EBV IgG)	In young males considered for thiopurine therapy
Varicella-zoster virus (anti VZV IgG)	In patients considered for JAK inhibitors
Tuberculin skin test	TB-Quantiferon (IGRA) in immunosuppressed patients (on steroids or immunomodulators)
Chest X-Ray	

Algorithm 10: Vaccines in IBD patients

Vaccines in IBD Patients



*This delay may be reduced to 1 month in case of use of corticosteroids alone

